

PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Tirofiban 50 micrograms/ml solution for infusion

Tirofiban

Read all of this leaflet carefully before you start using this medicine, because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Tirofiban is and what it is used for
2. What you need to know before you use Tirofiban
3. How to use Tirofiban
4. Possible side effects
5. How to store Tirofiban
6. Contents of the pack and other information

1 WHAT TIROFIBAN IS AND WHAT IT IS USED FOR

Tirofiban is used to help assist the blood flow to your heart and to help prevent chest pain and heart attacks. It works by preventing platelets, cells found in the blood, from forming blood clots.

This medicine may also be used in patients whose heart vessels are dilated with a balloon (percutaneous coronary intervention or PCI). This is a procedure, possibly with implantation of a small tube (stent), to improve the blood flow to the heart.

Tirofiban is intended for use with aspirin and unfractionated heparin.

2 WHAT YOU NEED TO KNOW BEFORE YOU USE TIROFIBAN

Do not use Tirofiban

- If you are allergic to tirofiban or any of the other ingredients of this medicine (listed in section 6)
- If you are bleeding internally or have a history of bleeding internally within the last 30 days
- If you have a history of bleeding in the brain, brain tumor or abnormal blood vessels in the brain
- If you have severe uncontrolled high blood pressure (malignant hypertension)
- If you have a low blood platelet count (thrombocytopenia) or problems with blood clotting
- If you developed thrombocytopenia when you previously received treatment with Tirofiban or another medicine in the same group of medicines
- If you have a history of stroke within the last 30 days or any history of stroke with bleeding
- If you have been seriously injured or had a major operation within the last 6 weeks
- If you have severe liver disease

Your doctor will review your medical history to see if you are at an increased risk of any side effects associated with being given this medicine.

Warnings and precautions

Talk to your doctor or pharmacist before using Tirofiban, if you have or have had:

- any medical problems
- any allergies
- cardiopulmonary resuscitation (CPR), a biopsy, or a procedure to break up kidney stones within the last 2 weeks
- been seriously injured or had a major operation within the last 3 months

- an ulcer in the stomach or intestine (duodenum) within the last 3 months
- a recent bleeding disorder (within 1 year) such as bleeding in the stomach or intestine, or blood in your urine or stool
- recent spinal procedure
- a history or symptoms of splitting of the aorta (aortic dissection)
- uncontrolled high blood pressure (hypertension)
- an inflammation of the lining around your heart (pericarditis)
- an inflammation of the blood vessels (vasculitis)
- problems with the blood vessels in the back of your eye (retina)
- treatment with medications that help to prevent or dissolve blood clots
- kidney problems
- a special intravenous line inserted under your collar bone within the last 24 hours
- heart failure
- very low blood pressure due to a failing heart (cardiogenic shock)
- a liver disorder
- low blood count or anaemia

Other medicines and Tirofiban

In general, Tirofiban can be used with other medicines. Please tell your doctor if you are taking or have recently taken or might take any other medicines, including medicines obtained without a prescription, as some drugs may affect each other's action. It is especially important to tell your doctor if you are taking other medicines that help prevent your blood from clotting such as warfarin.

Tirofiban with food and drink

Food and drink have no effect on this medicine.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Due to your disease state, you will not be able to drive or operate machinery while Tirofiban is being used.

Tirofiban contains sodium

This medicine contains 916.28 mg sodium (main component of cooking/table salt) in each 250 ml bag. This is equivalent to 46 % of the recommended maximum daily dietary intake of sodium for an adult.



The following information is intended for healthcare professionals only:

This product is for hospital use only, by specialist physicians experienced in the management of acute coronary syndromes.

Tirofiban should be administered with unfractionated heparin and oral antiplatelet therapy, including acetylsalicylic acid (ASA).

Posology and method of administration

In patients who are managed with an early invasive strategy for Non-ST-Segment Elevation Acute Coronary Syndrome (NSTEMI-ACS) but not planned to undergo angiography for at least 4 hours and up to 48 hours after diagnosis, Tirofiban is given intravenously at an initial infusion rate of 0.4 microgram/kg/min for 30 minutes. At the end of the initial infusion, Tirofiban should be continued at a maintenance infusion rate of 0.1 microgram/kg/min. Tirofiban should be given with unfractionated heparin (usually an intravenous bolus of 50-60 Units (U)/kg simultaneously with the start of Tirofiban therapy, then approx. 1000 U per hour, titrated on the basis of the activated partial thromboplastin time (APTT), which should be about twice the normal value) and oral antiplatelet therapy, including but not limited to ASA, unless contraindicated.

In NSTEMI-ACS patients planned to undergo PCI within the first 4 hours of diagnosis or in patients with acute myocardial infarction intended for primary PCI, Tirofiban should be administered utilising an initial bolus of 25 microgram/kg given over a 3 minute period, followed by a continuous infusion at a rate of 0.15 microgram/kg/min for 12-24, and up to 48 hours. Tirofiban should be administered with unfractionated heparin (dosage as above) and oral antiplatelet therapy, including but not limited to ASA, unless contra-indicated.

No dosage adjustment is necessary for the elderly.

Patients with severe kidney failure

In severe kidney failure (creatinine clearance < 30 ml/min) the dosage of Tirofiban should be reduced by 50%.

Paediatric population

The safety and efficacy of Tirofiban in children have not been established.

No data are available.

Start and duration of Tirofiban

In patients who are managed with an early invasive strategy for NSTEMI-ACS but not planned to undergo angiography for at least 4 hours and up to 48 hours after diagnosis, the Tirofiban 0.4 microgram/kg/min loading dose regimen should be initiated upon diagnosis. The recommended duration of the maintenance infusion should be at least 48 hours. Infusion of Tirofiban and unfractionated heparin may be continued during coronary angiography and should be maintained for at least 12 hours and not more than 24 hours after angioplasty/atherectomy. Once a patient is clinically stable and no coronary intervention is planned by the treating physician, the infusion should be discontinued. The entire duration of treatment should not exceed 108 hours.

If the patient diagnosed with NSTEMI-ACS and managed with an invasive strategy undergoes angiography within 4 hours after the diagnosis, the Tirofiban 25 microgram/kg dose bolus regimen should be initiated at the start of PCI with the infusion continued for 12-24 hours and up to 48 hours. In patients with acute myocardial infarction intended for primary PCI, the bolus infusion regimen should be initiated as soon as possible after diagnosis.

Concurrent therapy (unfractionated heparin, oral antiplatelet therapy including ASA)

Treatment with unfractionated heparin is initiated with an intravenous bolus of 50-60 U/kg and then continued with a maintenance infusion of 1000 units per hour. The heparin dosage is titrated to maintain an APTT of approximately twice the normal value.

Unless contraindicated, all patients should receive oral antiplatelet agents, including but not limited to ASA, before the start of Tirofiban. This medication should be continued at least for the duration of the infusion of Tirofiban.

Most studies investigating the administration of Tirofiban as an adjunct to PCI have used ASA in combination with clopidogrel as oral antiplatelet therapy. The efficacy of the combination of Tirofiban with either prasugrel or ticagrelor has not been established in randomised controlled trials

If angioplasty (PCI) is required, heparin should be stopped after PCI, and the sheaths should be withdrawn once coagulation has returned to normal, e.g. when the activated clotting time (ACT) is less than 180 seconds (usually 2-6 hours after discontinuation of heparin).

Incompatibilities

Incompatibility has been found with diazepam. Therefore, Tirofiban and diazepam should not be administered in the same intravenous line.

No incompatibilities have been found with Tirofiban and the following intravenous formulations: atropine sulfate, dobutamine, dopamine, epinephrine HCl, furosemide, heparin, lidocaine, midazolam HCl, morphine sulfate, nitroglycerin, potassium chloride, propranolol HCl, and famotidine injection.

Instructions for use

Check the expiry date.
Do not withdraw solution directly from the container with a syringe.

Directions for Use of Containers

Do not use unless solution is clear and bag is intact.

Do not add supplementary medication or withdraw solution directly from the bag with a syringe.
CAUTION: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

3. HOW TO USE TIROFIBAN

Tirofiban should be prescribed by a qualified doctor who is experienced in the management of heart attacks.

You have been given, or are about to be given, Tirofiban into a vein. Your doctor will decide on the appropriate dose, depending on your condition and your weight.

Use in children

The use in children is not recommended.

If you use more Tirofiban than you should

Your dose of Tirofiban is carefully monitored and checked by your doctor and pharmacist.

The most frequently reported symptom of overdose is bleeding. If you notice bleeding, you should notify your health care professional immediately.

If you forget to use Tirofiban

Your doctor will decide when to administer the dose.

If you stop using Tirofiban

Your doctor will decide when treatment should be stopped. However, if you wish to stop your treatment earlier, you should discuss other options with your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The most common side effect of treatment with Tirofiban is bleeding which could occur anywhere in the body. This can become serious and may rarely be fatal.

If side effects occur, they may need medical attention. While using Tirofiban, if you develop any of the following symptoms, you should contact your doctor immediately:

- Signs of bleeding in the skull such as pain in the head, sensory impairments (visual or hearing), difficulties in speech, numbness or problems with movement or balance
- Signs of internal bleeding such as coughing up blood or blood in your urine or stool
- Signs of serious allergic reactions such as difficulties in breathing and dizziness

Below is a list of side effects that have occurred in some people following treatment with Tirofiban. The side effects are listed in decreasing order of frequency.

Very common (may affect more than 1 in 10 people)

- Bleeding after surgery
- Bleeding under the skin at the site of an injection, or into a muscle, causing swelling
- Small red bruises on the skin
- Invisible blood in urine or stool
- Feeling sick
- Headache

Common (may affect up to 1 in 10 people)

- Blood in urine
- Coughing up of blood
- Nose bleeds
- Bleeding in the gums and mouth
- Bleeding from vessel puncture site
- Reduction in red blood cells (reduced haematocrit and haemoglobin)
- Decreases in platelet count below 90,000/mm³
- Fever

Uncommon (may affect up to 1 in 100 people)

- Bleeding in the stomach or intestines
- Vomiting of blood
- Decreases in platelet count below 50,000/mm³

Not known (frequency cannot be estimated from the available data)

- Bleeding in the skull
- Haematoma in the spinal region
- Bleeding in the abdomen of the internal organs
- Accumulation of blood around the heart
- Bleeding in the lung
- Acute and/or severe decreases in platelet counts below <20,000/mm³
- Severe allergic reactions with tightness of chest, hives or nettle rash, including reactions that cause difficulty in breathing and dizziness.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE TIROFIBAN

Your doctor or pharmacist will know how to store and dispose of this medicine. Keep this medicine out of the sight and reach of children.

After opening, the product should be used immediately.

Do not use Tirofiban after the expiry date which is stated on the bag. The expiry date refers to the last day of that month.

Do not use Tirofiban if there are visible particles or discolouration of the solution before use.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Tirofiban contains

The active substance is tirofiban.

Each 1 ml of solution for infusion contains 50 micrograms of tirofiban.

The other ingredients are: sodium acetate trihydrate, acetic acid, sodium chloride, sodium hydroxide (for pH adjustment) and water for injection.

What Tirofiban looks like and contents of the pack

Tirofiban is a clear, colourless solution available in 250 ml bags.

Pack sizes: 1 or 3 bags with 250 ml solution for infusion.

Not all pack sizes may be marketed

Marketing Authorisation Holder

Ibigen S.r.l.

Via Fossignano, 2

04011 – Aprilia (LT)

Italy

Manufacturer

Altan Pharmaceuticals, S.A.

Polígono Industrial de Bernedo, s/n

01118 Bernedo (Álava)

Spain

This leaflet was last revised in February 2020



Use according to the dosage table. The following table is provided as a guide to dosage adjustment by weight

Patient Weight (kg)	0.4 microgram/kg/min Loading Dose Regimen Most Patients		0.4 microgram/kg/min Loading Dose Regimen Severe Kidney Failure		25 microgram/kg Dose Bolus Regimen Most Patients		25 microgram/kg Dose Bolus Regimen Severe Kidney Failure	
	30 min Loading Infusion Rate (ml/hr)	Maintenance Infusion Rate (ml/hr)	30 min Loading Infusion Rate (ml/hr)	Maintenance Infusion Rate (ml/hr)	Bolus (ml)	Maintenance Infusion Rate (ml/hr)	Bolus (ml)	Maintenance Infusion Rate (ml/hr)
30-37	16	4	8	2	17	6	8	3
38-45	20	5	10	3	21	7	10	4
46-54	24	6	12	3	25	9	13	5
55-62	28	7	14	4	29	11	15	5
63-70	32	8	16	4	33	12	17	6
71-79	36	9	18	5	38	14	19	7
80-87	40	10	20	5	42	15	21	8
88-95	44	11	22	6	46	16	23	8
96-104	48	12	24	6	50	18	25	9
105-112	52	13	26	7	54	20	27	10
113-120	56	14	28	7	58	21	29	10
121-128	60	15	30	8	62	22	31	11
129-137	64	16	32	8	67	24	33	12
138-145	68	17	34	9	71	25	35	13
146-153	72	18	36	9	75	27	37	13

- Where the solution and container permit, parenteral drugs should be inspected for visible particles or discolouration before use
- Tirofiban should only be given intravenously and may be administered with unfractionated heparin through the same infusion tube
- It is recommended that Tirofiban be administered with a calibrated infusion set using sterile equipment
- Care should be taken to ensure that no prolongation of the infusion of the initial dose occurs and that miscalculation of the infusion rates for the maintenance dose on the basis of the patient's weight is avoided